Executive Summary

Application Type	NDA 21-114 NDA 20-816
Submission Number	002
Submission Code	SE8
Letter Date	3/27/2006
Stamp Date	3/28/2006
PDUFA Goal Date	9/26/2006
Reviewer Name	Jennifer Harris, M.D.
Review Completion Date	7/20/06
Established Name	levobetaxolol hydrochloride ophthalmic suspension brinzolamide ophthalmic suspension
Trade Name	Betaxon 0.5% Azopt 1%
Therapeutic Class	beta-blocker carbonic anhydrase inhibitor
Applicant	Alcon Research, Ltd.
Priority Designation	P
Formulation	ophthalmic suspension
Dosing Regimen	Betaxon – one drop twice day Azopt – one drop three times a day
Indication	treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma
Intended Population	pediatric patients less than 6 y.o.

1 EXECUTIVE SUMMARY

1.1 Recommendation on Regulatory Action

NDA 21-114/SE8 is recommended for approval after labeling revisions are made consistent with the recommendations listed in this review. The clinical study contained in this supplement supports the use of levobetaxolol hydrochloride ophthalmic suspension in the pediatric population. The benefits of using this drug product outweigh the risks in the treatment of elevated intraocular pressure in pediatric patients.

NDA 21-816/SE8 is recommended to be approved with revised labeling describing the failure of the b.i.d dosing regime. The clinical data generated in the amendment is not sufficient to establish the safety or efficacy of brinzolamide ophthalmic suspension in the pediatric population.

1.2 Recommendation on Postmarketing Actions

N/A – there are no recommendation on postmarketing actions

1.2.1 Risk Management Activity

N/A – there are no recommendations for risk management activity

1.2.2 Required Phase 4 Commitments

N/A – there are no recommended Phase 4 commitments

1.2.3 Other Phase 4 Requests

It is recommended that Azopt (brinzolamide ophthalmic suspension) 1% be studied in pediatric patients when dosed three times a day.

1.3 Summary of Clinical Findings

1.3.1 Brief Overview of Clinical Program

Clinical study C-00-17 was conducted to obtain needed pediatric information on Azopt (brinzolamide ophthalmic suspension), 1% and Betaxon (levobetaxolol hydrochloride ophthalmic suspension), 0.5% for the treatment of elevated intraocular pressure in children less than 6 years of age. This study was conducted in response to the Agency's Written Request of October 15, 1999, as amended November 17, 2000, May 16, 2003 and August 30, 2004, and re-issued July 02, 2002 and May 07, 2004 for AZOPT 1%. It

was also conducted in response to the Agency's Written Request of October 15, 1999, as amended November 17, 2000, May 16, 2003 and August 30, 2004, and re-issued July 03, 2002 and May 10, 2004 for Betaxon 0.5%. This study was also conducted to fulfill the requirements of 21 CFR§314.55 for Betaxon. Deferred submission of pediatric data was granted in the approval letter for Betaxon dated February 23, 2000 and in the Agency's letter of May 26, 2004.

Study C-00-17 was designed to describe the safety and clinical response of AZOPT 1% and Betaxon 0.5% in patients 0 to 5 years of age with a clinical diagnosis of glaucoma or ocular hypertension. The clinical safety and efficacy of AZOPT 1% and BETAXON 0.5% have been established in adult and elderly patients with glaucoma or ocular hypertension in NDA 20-816 [Azopt (brinzolamide ophthalmic suspension), 1%] and NDA 21-114 [Betaxon (levobetaxolol hydrochloride ophthalmic suspension), 0.5%], respectively.

The pediatric clinical development plan for Azopt and for Betaxon included one safety/efficacy study (C-00-17). The objective of study C-00-17 was to describe the safety and IOP-lowering ability of Azopt 1% and Betaxon 0.5% in children less than 6 years of age with glaucoma or ocular hypertension.

This submission is based on data from a total of 32 pediatric patients exposed to Azopt and 48 exposed to Betaxon.

1.3.2 Efficacy

The purpose of the trial contained in this pediatric supplement was to demonstrate the safety of levobetaxolol HCL and brinzolamide when used in pediatrics patients below the age of six. The support for efficacy for both of these products was extrapolated from the adult trials. The limited clinical response data contained in the supplement demonstrates that levobetaxolol lowered IOP by approximately 1-2 mmHg while brinzolamide lowered IOP by approximately 0-2 mmHg.

1.3.3 Safety

- *The study in this NDA amendment is adequate to establish the safety of the use of levobetaxolol hydrochloride ophthalmic suspension in the pediatric population.*

- *The type of adverse events seen in patients treated with levobetaxolol are consistent with those seen in the adult population.*

- *There were no clinically relevant differences in the adverse event profile between the age group strata that were studied (i.e. 1 week to < 1 year, 1 year to < 2 years, 2 years to < 4 years, and 4 years to < 6 years.*

- *There was inadequate safety data gathered in this trial to support the use of Azopt in the pediatric population.*

1.3.4 Dosing Regimen and Administration

The dosage and administration in the pediatric population is identical to that which has been established in the adult population. The sponsor has not submitted data to support any change in the already established dose and frequency for either of these two products.

1.3.5 Drug-Drug Interactions

Drug/drug interaction analyses were not conducted for this trial.

1.3.6 Special Populations

There are no important considerations required for administering this product in special populations. The pediatric subpopulations analyzed were 1 week to < 1 year, 1 year to < 2 years, 2 years to < 4 years and 4 years to < 6 years of age. Adverse events and the safety profile for levobetaxolol hydrochloride and brinzolamide were consistent between these age groups.

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/s/

Jennifer Harris
9/11/2006 11:30:22 AM
MEDICAL OFFICER

William Boyd
9/11/2006 11:37:28 AM
MEDICAL OFFICER